Hemolytic Uremic Syndrome (HUS)

1. DISEASE REPORTING

A. Purposes of Reporting and Surveillance

1. To identify hemolytic uremic syndrome (HUS) cases as possible indicators of *E. coli* O157:H7 cases in the community, since HUS is a severe complication of infection with *E. coli* O157:H7 or less commonly other pathogens.
2. To identify outbreaks and potential sources of ongoing transmission, and to prevent further transmission from such sources.
3. To educate people about how to reduce their risk of infection.

B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction.**
2. Hospitals: **immediately notifiable to local health jurisdiction**.
3. Laboratories: no requirements for reporting.
4. Local health jurisdiction: **immediately notifiable to Communicable Disease Epidemiology Section (1-877-539-4344).**

C. Local Health Jurisdiction Investigation Responsibilities

1. Begin the investigation with one working day.
2. If stool shiga toxin assay and culture have not been performed, request that a stool specimen from the case of HUS be sent to PHL for culture to try to identify a causative agent.
3. Report all *probable* cases of HUS to CDES. Complete the HUS case report form (www.doh.wa.gov/notify/forms/hus.doc) and enter the data into the Public Health Issues Management System (PHIMS).
    a. Report HUS without a clear history of diarrhea or an identified pathogen as HUS.
    b. Report enterohemorrhagic *E. coli* with HUS as enterohemorrhagic *E. coli*.
    c. Report post-diarrheal HUS as suspect enterohemorrhagic *E. coli*.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

HUS is most commonly a complication of infection with *E. coli* O157:H7, but can occur following infection with other enterohemorrhagic (shiga toxin-producing) *E. coli* as well as *Shigella* and other bacterial pathogens. In rare situations, *E. coli* O157 is eventually confirmed as the cause of HUS or the related syndrome thrombotic thrombocytopenic purpura (TTP) in cases without antecedent diarrheal illness.

B. Description of Illness

Hemolytic uremic syndrome (HUS) occurs as a complication in 2–7% of diagnosed *E. coli* O157:H7 cases, particularly children, and less commonly after other infections. The syndrome is characterized by microangiopathic hemolytic anemia, acute renal failure, and thrombocytopenia. Early clinical signs of HUS may include decreased urine output, pallor, and lethargy. Patients with HUS have a variable degree of renal insufficiency that may necessitate kidney dialysis (short- or long-term) or even total renal failure; there is also an increased risk of stroke and other complications. TTP, another complication of *E. coli* O157:H7 infection which primarily affects adults, resembles HUS but also includes fever and neurologic signs such as seizures or confusion.

C. HUS in Washington State

Hemolytic uremic syndrome first became a notifiable condition in Washington in December 2000. Since then, 1–6 cases have been reported to DOH per year. Cases with HUS and a confirmed agent are reported under the specific agent. Cases with HUS and diarrhea without a confirmed agent are reported as suspect enterohemorrhagic *E. coli.*

D. Reservoir

E. coli are ubiquitous in the intestines of warm-blooded vertebrates while *Shigella* occur only in humans. *E. coli* are Gram-negative bacteria classified by the letters "O" (cell wall) and "H" (flagellar) antigens. Most *E. coli* serotypes are non-pathogenic. Enterohemorrhagic *E. coli* are also referred to as shiga toxin-producing *E. coli* (STEC) or sometimes Vero-toxin producing *E. coli* (VTEC). In Washington and the rest of North America, the most common STEC is *E. coli* O157:H7. Other less common STEC strains cause similar illnesses.

E. Modes of Transmission

Transmission of the agents is fecal-oral, for *E. coli* O157:H7 most commonly through ingestion of contaminated food, or direct contact with animals such as on farms or at petting zoos. The infectious dose is very low for *E. coli* O157:H7. Undercooked beef (especially hamburger), other foods cross-contaminated from raw beef, and raw milk are the prototypical causes of common-source outbreaks, reflecting the fact that these foods are likely to be contaminated with cattle manure. Venison is another potential source.

Contaminated produce, including lettuce, alfalfa sprouts, and unpasteurized apple cider are other well-recognized sources. Person-to-person transmission also occurs, either directly (households, child care centers, institutions) or indirectly (contaminated drinking or recreational water).

F. Incubation Period

In cases of *E. coli* O157:H7, HUS occurs 2–14 days after onset of diarrhea.

G. Period of Communicability

Varies with agent, for *E. coli* O157:H7 typically less than one week for adults and up to three weeks for one third of children. A documented culture negative case of HUS is assumed noncommunicable.

H. Treatment

It is reported that treatment of *E. coli* O157:H7 infections with some antibiotics may precipitate HUS. Treatment of HUS is supportive, including hydration and when appropriate kidney dialysis.

3. CASE DEFINITIONS

A. Clinical Criteria for Diagnosis

Hemolytic uremic syndrome (HUS) is characterized by the acute onset of microangiopathic hemolytic anemia, renal injury, and low platelet count. Thrombotic thrombocytopenic purpura (TTP) also is characterized by these features but can include central nervous system (CNS) involvement and fever and may have a more gradual onset. Most cases of HUS (but few cases of TTP) occur after an acute gastrointestinal illness (usually diarrheal); post-diarrheal HUS without a specific agent identified is reported as suspect *E. coli* O157:H7.

B. Laboratory Criteria for Diagnosis

The following are both present at some time during the illness:

- Anemia (acute onset) with microangiopathic changes (i.e., schistocytes, burr cells, or helmet cells) on peripheral blood smear **and**
- Renal injury (acute onset) evidenced by hematuria, proteinuria, or elevated creatinine level (i.e., ≥ 1.0 mg/dL in a child aged <13 years or ≥ 1.5 mg/dL in a person aged ≥ 13 years, or ≥ 50% increase over baseline).

Note: A low platelet count can usually, but not always, be detected early in the illness, but it may then become normal or even high. If a platelet count obtained within 7 days after onset of the acute gastrointestinal illness is not <150,000/mm3, other diagnoses should be considered.

C. Case Definition

Probable

- An acute illness diagnosed as HUS or TTP that both meets the laboratory criteria and does not follow an episode of acute or bloody diarrhea in the preceding 3 weeks **or**
- An acute illness diagnosed as HUS or TTP that a) has onset within 3 weeks after onset of an acute or bloody diarrhea and b) meets the laboratory criteria except that microangiopathic changes are not confirmed.

Note: HUS following diarrhea, formerly reported as confirmed HUS, is now reported as suspect enterohemorrhagic *E. coli.* Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore, criteria for diagnosing TTP on the basis of CNS involvement and fever are not provided because cases diagnosed clinically as postdiarrheal TTP also should meet the criteria for HUS. These cases are reported as suspect enterohemorrhagic *E. coli*.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Demonstration of acute anemia with microangiopathic changes based on:

1) complete blood count (CBC) with examination of the peripheral blood smear **and**

2) acute renal injury based on urinalysis showing hematuria or proteinuria or on elevated serum creatinine level (i.e., ≥ 1.0 mg/dL in a child aged <13 years or ≥ 1.5 mg/dL in a person aged ≥ 13 years, or ≥ 50% increase over baseline) **and**

3) if tested, stool negative for enteric pathogens and for shiga toxin.

B. Tests Available at DOH Public Health Laboratories (PHL)

Blood counts, urinalysis, and serum creatinine tests are commercially available. PHL can provide stool testing for enterohemorrhagic *E. coli* and can confirm *E. coli* O157:H7 isolates.

C. Criteria for Testing at PHL

PHL provides stool culturing for enterohemorrhagic *E. coli* in potential outbreak situations. Non-O157 enterohemorrhagic *E. coli* are serotyped at the PHL or sent to CDC for further identification. Serologic tests for antibody levels are available at CDC in special circumstances; consult CDES for more details.

D. Specimen Collection

For stool culture, use a sterile applicator swab to collect stool, insert the swab into Cary-Blair transport medium, push the cap on tightly, label the tube, and mail immediately.

Please enclose a completed PHL Enteric Bacteriology form (available at: http://www.doh.wa.gov/EHSPHL/PHL/Forms/EntericBacteriology.pdf) with all isolates and stool specimens.

5. ROUTINE CASE INVESTIGATION

A single case of HUS may be an indicator of an outbreak since only about 5% of *E. coli* O157:H7 infections progress to HUS. It is important to identify other potential infections and obtain diagnostic tests.

A. Confirm the Diagnosis

If a stool shiga toxin assay and culture have not been performed at an outside laboratory, a stool specimen should be sent to PHL for shiga toxin testing and culture to try to identify a causative agent.

B. Identify Potential Sources of Infection

HUS typically occurs 2–14 days after onset of diarrhea. Ask about possible exposures 1–2 weeks or longer before onset of symptoms, including:

1. Contact or household member with a diarrheal illness, whether occurring before, concurrent with, or after the case. Obtain the name, phone number or address and clinical information of the ill person. Anyone meeting the suspect or probable case definition for enterohemorrhagic *E. coli* should be reported and investigated in the same manner as a

case of enterohemorrhagic *E. coli.*

2. Handling or eating ground beef. Ask about consumption of undercooked hamburger (pink or red), but because of the possibility of cross-contamination any ground beef consumption is potentially suspect. Get details about any ground beef consumed (stores where purchased, dates of purchase, type of meat e.g., lean or extra-lean hamburger, frozen patties), and how handled/cooked. Any raw beef is potentially a source of kitchen contamination, but intact cuts of meat sold at retail are unlikely to cause multi-household outbreaks.
3. Consumption of unpasteurized milk. Identify the brands and/or sources, and find out when this milk consumption began. If a commercial raw milk source is named, notify CDES immediately.
4. Restaurant meals. Obtain the name of the restaurant, and date and location of the meal.
5. Public gathering where food was consumed. Obtain the date, location, and sponsor of the event.
6. Dried meats (particularly home prepared) are another possible source, as is anything related to deer or elk hunting (consumption, slaughtering, processing game).
7. Recreational water exposures: swimming, playing, or other exposure to lakes, streams, swimming or wading pools, where water may have been swallowed.
8. Contact with livestock, especially cattle, or animals such as at a petting zoo.
9. Contact with diapered children with diarrhea, or children in child care.
10. Raw, potentially contaminated produce including sprouts, lettuce, and unpasteurized apple juice or cider.
11. Occupational exposures: evaluate the potential for exposure to human or animal excreta.
12. Travel outside the local area.

C. Identify Contacts who Work in Sensitive Occupations

Determine if any household member or close contact attends or works at a child care facility; or works as a food handler or health care worker.

D. Environmental Evaluation

None, unless a commercial food service facility or product, child care center, or public water supply appears to be implicated as the source of infection.

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations

1. Hospitalized patients should be treated using standard precautions. Contact precautions should be used for diapered or incontinent persons for the duration of the illness or to control institutional outbreaks.
2. The case should be educated regarding effective hand washing, particularly after using the toilet, changing diapers, and before preparing or eating food.
3. Persons with a history of diarrhea should be managed as a suspect case of

enterohemorrhagic *E. coli* (see Reporting and Surveillance Guidelines for Enterohemorrhagic *E. coli*).

4. School Restrictions: Children with HUS and no history of diarrhea can return to school when they are feeling well.
5. Work and Child Care Restrictions: Work and child care restrictions of persons with HUS and no history of diarrhea who work as food handlers, child care or healthcare workers, or attend child care should be handled on case-by-case basis.

B. Contact Management

1. Symptomatic contacts: All contacts with symptoms compatible with enterohemorrhagic *E. coli* should be referred to a healthcare provider for assessment and laboratory testing. Contacts with symptoms consistent with EHEC who work as food handlers, healthcare workers, child care workers, or attend child care should be managed as EHEC cases.
2. Asymptomatic contacts: Cultures may be considered if an asymptomatic household member or other close contact works as a food handler, healthcare worker, child care worker, or attends child care.
3. Education: All contacts should be educated about transmission routes, symptoms, and effective hand washing, particularly after using the toilet, changing diapers, and before preparing or eating food.

C. Environmental Measures

If indicated, give advice on proper cooking and food handling practices to prevent infection.

7. MANAGING SPECIAL SITUATIONS

A. Possible Foodborne or Waterborne Outbreaks

Call CDES immediately if you suspect a common-source outbreak.

B. Case is a Child Care Worker or Attendee

1. Interview the operator and inspect attendance records to identify other possible cases among staff or attendees during the past month.
2. Review food handling, hand washing techniques, and diaper changing practices with the operator and staff.
3. Collect stool specimens for culture from any other attendees or staff with a history of diarrheal illness within the recent past.
4. If lab confirmed enterohemorrhagic *E. coli* or *Shigella* cases are identified, apply appropriate restrictions.
5. If more than one case or suspected case is identified among attendees or workers at a child care facility, inspect the facility.
6. Instruct the facility operator to call the LHJ immediately if new cases of diarrhea occur.
7. Make follow-up contact with the child care center to assure that surveillance and appropriate hygienic measures are being carried out.

C. Cases Linked to Raw Milk Products

Environmental evaluation of the dairy will be a necessary part of any further investigation. Dairy investigations will be conducted in cooperation with the Washington State Department of Agriculture.

8. ROUTINE PREVENTION

A. Vaccine Recommendations: None

B. Prevention Recommendations

Advise individuals on measures to avoid further or future exposures including:

1. Avoid eating raw or undercooked meat or poultry, especially hamburger. Hamburger prepared at home should be cooked to an internal temperature of at least 160 F. While it is best to use a thermometer, cook at least until there is no red or pink remaining and meat juices have no color.
2. Avoid cross-contamination with meat or other potentially contaminated foods.
3. Wash fruits and vegetables thoroughly before consumption. Peel when possible.
4. Wash hands after caring for diapered children, after using the toilet, and after handling soiled clothing or linens.
5. Wash hands after handling pets, fowl, other animals, raw meat, and raw poultry, and always before food preparation.
6. Avoid unpasteurized milk, and other unpasteurized products including soft cheese, juices, and cider.
7. Avoid drinking or swallowing untreated surface water. Untreated water should be boiled or otherwise disinfected before consumption
8. Persons with diarrhea should not prepare food for others.

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UPDATES